

Appl. No. 10/086,294  
Response to Restriction Requirement faxed 05 Nov 2004  
Reply to Restriction Requirement of October 6, 2004

PATENT

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Previously presented) A method of treating mammalian cancer cells deficient in functional p53, said method comprising contacting cells from said cancer cells with a p53 tumor suppressor protein or nucleic acid encoding p53 and also contacting said cells with a microtubule affecting agent, such that one or more disease characteristic of the cell is ameliorated, wherein the mammalian cancer cells are human head and neck, ovarian, prostate, or mammary cancer cells.
2. (Canceled)
3. (Previously presented) The method of claim 1 wherein said microtubule affecting agent is paclitaxel or a paclitaxel derivative.
4. (Original) The method of claim 1, wherein said method further comprises contacting a cell with a chemotherapeutic agent.
5. (Original) The method of claim 4, wherein said chemotherapeutic agent is cisplatin, carboplatin, or navelbine.
6. - 8. (Canceled)
9. (Original) The method of claim 1, wherein said nucleic acid is delivered by a vector selected from the group consisting of a naked DNA plasmid, a plasmid within a liposome, a plasmid complexed with a lipid, a viral vector, an AAV vector, and a recombinant adenoviral vector.

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10. (Original) The method of claim 1, wherein said nucleic acid is delivered by a recombinant adenoviral vector.

11. (Original) The method of claim 10, wherein said nucleic acid is delivered by a recombinant adenoviral vector comprising a partial or total deletion of a protein IX DNA and comprising a nucleic acid encoding a wild-type p53 protein.

12. (Original) The method of claim 11, wherein said deletion of the protein IX gene sequence extends from about 3500 bp from the 5' viral termini to about 4000 bp from the 5' viral termini.

13. (Original) The method of claim 12, further comprising deletion of a non-essential DNA sequence in adenovirus early region 3.

14. (Original) The method of claim 11, further comprising deletion of a non-essential DNA sequence in adenovirus early region 4.

15. (Original) The method of claim 11, further comprising a deletion of DNA sequence designated E1a and E1b.

16. (Original) The method of claim 10, wherein said recombinant adenoviral vector comprises the adenovirus type 2 major late promoter or the human CMV promoter, the adenovirus type 2 tripartite leader cDNA and a human p53 cDNA.

17. (Original) The method of claim 16, wherein said vector is A/C/N/53.

18. (Previously presented) The method of claim 1, wherein said microtubule affecting agent is selected from the group consisting of paclitaxel and Taxotere®.

19. (Previously presented) The method of claim 18, wherein said microtubule affecting agent is TAXOL®.

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20. (Previously presented) The method of claim 3, wherein said cells are first contacted with said p53 tumor suppressor protein or nucleic acid encoding p53 and are subsequently contacted with said paclitaxel or paclitaxel derivative.

21. (Previously presented) The method of claim 3, wherein said cells are first contacted with said paclitaxel or paclitaxel derivative and are subsequently contacted with said p53 tumor suppressor protein or nucleic acid encoding p53.

22. (Previously presented) The method of claim 3, wherein said cells are simultaneously contacted with said paclitaxel or paclitaxel derivative and with said p53 tumor suppressor protein or nucleic acid encoding p53.

23. - 24. (Canceled)

25. (Previously presented) The method of claim 1, wherein said p53 tumor suppressor protein or nucleic acid encoding p53 is dispersed in a pharmacologically acceptable excipient.

26. (Previously presented) The method of claim 3, wherein said paclitaxel or paclitaxel derivative is dispersed in a pharmacologically acceptable excipient.

27. (Previously presented) The method of claim 3, wherein said p53 tumor suppressor protein or nucleic acid encoding p53 and said paclitaxel or paclitaxel derivative are dispersed in a single composition.

28. (Previously presented) The method of claim 1, wherein said contacting comprises injecting said p53 tumor suppressor protein or nucleic acid encoding p53 into a tumor.

29. (Previously presented) The method of claim 1, wherein said contacting comprises intra-arterial injection of said p53 tumor suppressor protein or nucleic acid encoding p53.

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30. (Previously presented) The method of claim 29, wherein said contacting comprises intraperitoneal administration of said p53 tumor suppressor protein or nucleic acid encoding p53 for the treatment of ovarian cancer.

31. (Original) The method of claim 3, wherein said contacting comprises injecting said paclitaxel or paclitaxel derivative into a tumor.

32. (Original) The method of claim 3, wherein said contacting comprises intravenously injecting said paclitaxel or paclitaxel derivative.

33. (Original) The method of claim 1, wherein said contacting comprises systemic, regional, local, topical, intraperitoneal, intra-pleural cavity, oral, buccal, sublingual, intra-tracheal, transmucosal, bladder, vaginal, uterine, rectal, or nasal administration.

34. (Previously presented) The method of claim 3, comprising contacting said cells with A/C/N/53 and paclitaxel.

35. (Previously presented) The method of claim 1, wherein said contacting cells with a p53 tumor suppressor protein or nucleic acid encoding p53 comprises contacting said cells with said p53 tumor suppressor protein or nucleic acid encoding p53 in a multiplicity of treatments each separated by at least about 6 hours.

36. (Original) The method of claim 1, wherein said method comprises at least three treatments separated by about 24 hours.

37. (Previously presented) The method of claim 3, wherein:  
said p53 tumor suppressor protein or nucleic acid encoding p53 is administered in a total dose ranging from about  $1 \times 10^9$  to about  $7.5 \times 10^{15}$  adenovirus particles in a treatment regimen selected from the group consisting of: the total dose in a single dose, the total dose divided over 5 days and administered daily, the total dose divided over 15 days and administered daily, and the total dose divided over 30 days and administered daily; and

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said paclitaxel or paclitaxel derivative is administered in a total dose ranging from about 75 to about 350 mg/m<sup>2</sup> over 24 hours in a treatment regimen selected from the group consisting of administration in a single dose, in a dose administered daily on day 1 and day 2, in a dose administered daily on day 1, day 2, and day 3, on a daily dosage for 15 days, on a daily dosage for 30 days, on daily continuous infusion for 15 days, on daily continuous infusion for 30 days.

38. (Original) The method of claim 37, wherein said method is repeated for two or more cycles.

39. (Original) The method of claim 38, wherein said two or more cycles are spaced apart by three or four weeks.

40. (Original) The method of claim 38, wherein said method is repeated for three cycles.

41. - 77. (Canceled)

78. (Previously presented) A method of treating human head and neck, ovarian, prostate, or mammary cancer cells in a mammal, the method comprising administering to the mammal a p53 tumor suppressor protein or nucleic acid sequence encoding a p53 tumor suppressor protein and also administering to the animal a microtubule affecting agent, such that one or more disease characteristics of the cancer cells is ameliorated.

79. (Previously presented) A method of treating human head and neck, ovarian, prostate, or mammary cancer cells *in vitro*, the method comprising contacting cells from the cancer cells with a p53 tumor suppressor protein or nucleic acid sequence encoding a p53 tumor suppressor protein and also contacting the cells with a microtubule affecting agent, such that one or more disease characteristics of the cancer cells is ameliorated.